## Remarks/Arguments

The foregoing amendments to the claims are of a formal nature, and do not add new matter. Claim 123 has been canceled without prejudice or disclaimer. Thus, Claims 124-126, 129-131 and 135-138 are pending in this application. The rejections to the presently pending claims are respectfully traversed.

## Claim Rejections – 35 USC § 101 and 112, first paragraph- Enablement

Claims 123, 124, 129-131, 135-138 are rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility."

Claims 123, 124, 129-131, 135-138 are further rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention".

The Examiner asserts that the Goddard declaration is insufficient to overcome the rejection and adds that "Applicants arguments regarding TaqMan PCR are not deemed persuasive because it only shows that the instant specification provides an invitation to experiment, and not a readily available utility." The Examiner also adds that "the PRO1185 nucleic acid was amplified in some cancers, to a minor degree (about 2.5-3.0 fold). No mutation or translocation of PRO1185 has been associated with any type of cancer versus normal tissue....One cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in **transcription rates**. It remains that, as evidenced by Pennica the issue is simply not predictable, and the specification presents a mere invitation to experiment". Regarding the Goddard declaration, he Examiner further quotes Hu *et al.* to show that "the literature cautions researchers from drawing conclusions **based on small changes in transcript expression levels between normal and cancerous tissue**" (Emphasis added). For the reasons outlined below, Applicants respectfully disagree.

**Arguments**

The Utility guidelines were reviewed in the previous response. PRO1185 showed approximately 1.01, 1.66 and 1.58 ΔCt units which corresponds to **2.013, 3.160, 2.989-fold** amplification in lung tumors. Based on these positive results, Applicants had asserted that the PRO1185 gene has utility as a diagnostic marker for lung cancer. Applicants had also submitted the Goddard declaration, an expert's declaration to show that a 2-fold amplification is considered significant.

As a preliminary matter, Applicants draw the Examiner's attention to the instant claims directed to nucleic acids of PRO1185 based on the gene amplification data. Therefore rejections based on "mRNA" or "transcription rates" or on the reference Hu *et al.* that measures and addresses mRNA data bear no relevance to the present claims.

Further, Applicants submit that the case law has clearly established that in considering affidavit evidence, the Examiner must consider all of the evidence of record anew. [1] "After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of the evidence with due consideration to persuasiveness of argument" [2] Furthermore, the Federal Court of Appeals held in *In re Alton*, "[w]e are aware of no reason why opinion evidence relating to a fact issue should not be considered by an examiner" [3]. Applicants also respectfully draw the Examiner's attention to the Utility Examination Guidelines [4] which states that, "Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered". The statement in question from an expert in the field (the Goddard declaration) states:

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[1] *In re Rinehart 531* F.2d 1084, 189 USPQ 143 (CCPA 1976) and *In re Piasecki* 745 F 2d. 1015, 226 USPQ 881 (Fed. Cir. 1985).

[2] *In re Alton* 37 USPQ2d 1578 (Fed. Cir 1966) at 1584 quoting *In re Oetiker* 977 F 2d at 1445, u2 USPQ2d at 1444.

[3] *In re Alton*, supra.

[4] Part IIB, 66 Fed. Reg. 1098 (2001).

"It is my personal experience that the quantitative TaqMan PCR technique is technically sensitive enough to detect at least a 2-fold increase in gene copy number relative to control. It is further my considered scientific opinion that an at least 2-fold increase in gene copy number in a tumor tissue sample relative to a normal (i.e., non-tumor) sample is significant and useful in that the detected increase in gene copy number in the tumor sample relative to the normal sample serves as a basis for using relative gene copy number as quantitated by the TaqMan PCR technique as a diagnostic marker for the presence or absence of tumor in a tissue sample of unknown pathology. Accordingly, a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring the efficacy of cancer therapy."

Therefore, barring evidence to the contrary from the Examiner regarding the above statement in the Goddard declaration, this rejection is improper under both the case law and the Utility guidelines.

Applicants also submit that the gene amplification data shows that the nucleic acid encoding for PRO1185 is amplified in lung tumors, regardless of the mechanism by which this amplification occurs and provides a readily available utility. As the M.P.E.P. §2107.01 cautions, **"Office personnel must be careful not to interpret the phrase "immediate benefit to the public"** or similar formulations used in certain court decisions **to mean that products or services based on the claimed invention must be "currently available" to the public** in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a '"substantial" utility'"[5] (emphasis added). Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement states, "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." Applicants respectfully submit that The Utility guidelines do not require a showing of the precise mechanism for the utility as long as there is

[5] *Id.* at 534, 148 U.S.P.Q. (BNA) at 695.

utility for the invention and one skilled in the art would find the utility reasonable based on the data. The TaqMan PCR assay or the gene amplification results described in detail for PRO1185 nucleic acids in the specification provide specific, substantial and credible utility for detecting lung tumors. Therefore, as long as the instant nucleic acids are useful as diagnostic tools based on the TaqMan PCR results, the instant application fulfills the utility requirement. This utility is fully enabled by the instant specification and therefore one skilled in the art would know how to make and use the nucleic acids encoding PRO1185 for detecting lung tumors.

In conclusion, Applicants have demonstrated a credible, specific and substantial asserted utility for the PRO1185 nucleic acid based on the gene amplification results, for example, in detecting over-expression of PRO1185. Accordingly, the present 35 U.S.C. §101 and §112, first paragraph utility rejections should be withdrawn.

**Priority**

For the reasons discussed in the previous response, Applicants maintain that they rely on the gene amplification assay for patentable utility in this case. This utility was first disclosed in International Application PCT/US00/03565, filed February 11, 2000, priority to which has been claimed in this application. Hence, Applicants are at least entitled to an effective filing date of **February 11, 2000** for the present application.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C69).

Respectfully submitted,

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